REMARKS

The Examiner provides a number of rejections. We list them here in the order in which they are addressed.

I. Claims 1, 9, 11-12 and 38-41 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Little *et al.* (U.S. Patent No. 6,207,370) in view of Garvin *et al.* (U.S. Patent No. 6,329,180) and further in view of Nakajima *et al.* and Hosfield *et al.*

II. Claims 1, 9, 11-13 and 38-41 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Little *et al.* (U.S. Patent No. 6,207,370) in view of Garvin *et al.* (U.S. Patent No. 6,329,180) further in view of Nakajima *et al.* and Hosfield *et al.* and further in view of Elion *et al.*

Applicants respond as follows:

I. Claims 1, 9, 11-12 and 38-41 are not unpatentable under 35 U.S.C. §103(a).

The Claims are rejected as obvious over Little *et al.* in view of Garvin *et al.* and further in view of Nakajima *et al.* and Hosfield *et al.* Applicants disagree.

The Examiner has admitted (in the last two office actions) that neither Little *et al.* nor Garvin *et al.* teach a primer with two epitope markers. The Examiner attempted to remedy this deficiency (in a previous office action) with Knop *et al.* In response to the Applicants' demonstration that the primers of Knop *et al.* do not contain a single - let alone two - epitope markers, the Examiner now cites two new references that allegedly teach this still missing element. In addition to the increasingly evident hindsight driven nature of this prosecution (discussed below), the Applicants emphasize that Nakajima *et al.* and Hosfield *et al.* fail to remedy the deficiencies of record; even if the combination of these references were proper – which it is not.

a) Nakajima *et al.* is completely unrelated to the present claims and cannot remedy the deficiencies of Little *et al.* and Garvin *et al.* - even IF the combination were permissible.

The Examiner's entire analysis of Nakajima *et al.* is as follows:

> Nakajima et al teach multi-epitope tag sequences in primers. The primer contains tandem repeat myc sequences. However, they do not teach that the tags are different from each other. *Office Action, page. 5, lines 12-14.*

The Applicants cannot understand how these primers have any relevance to those of the present claims. Nakajima *et al.* merely discloses a method of constructing a multiple-epitope tag using primers that hybridize to each other such that successive rounds of amplification produce increasingly large myc tags. As evidenced throughout this reference, and shown schematically in Figure 1 of the reference, the PCR reactions of Nakajima *et al.* include ONLY primers. These forward and reverse primers are simply c-myc domains that partially hybridize to each other at their respective 3' ends, thereby serving as their own template! A successive round of amplification produce increasingly long c-myc template repeats; which are later attached to a protein of interest.

How exactly would a skilled artisan find it obvious to remedy the admitted deficiencies of Little *et al.* and Garvin *et al.* by looking to Nakajima *et al.*? The present invention seeks to introduce different tags for different purposes in the context of a nascent protein: one to permit attachment, one to permit detection of the N-terminus, one to permit detection of the C-terminus. The Examiner acknowledges that the epitope tags of Nakajima *et al.* are not different from each other. The reference merely teaches increased Western blot sensitivity by using self-annealing primers that produce nothing more than a plurality of identical epitope tags. Thus, Nakajima *et al.* are not in the same field of endeavor.[1] Furthermore, it does not address the problem solved by the three different tags of the present invention. This makes Nakajima *et al.* non-analogous art and therefore improper art for an obviousness rejection. For this reason, Applicants ask that the rejection be withdrawn.

b) The cloning vector of Hosfield *et al.* does nothing to remedy the admitted deficiency of Nakajima *et al.*

The Examiner's entire analysis of Hosfield *et al.* is as follows:

> Hosfield et al teach an epitope-tagging vector with two different epitope markers. The

[1] Merely, because the reference deals with biotechnology does not make it in the same field of endeavor. See In re Clay, 966 F.2d 656 (Fed. Cir. 992) (the reference is not in the same "field of endeavor merely because both relate to the petroleum industry.")

> vector contains a FLAG and c-myc epitope. Figure 1 shows that the markers are 3' of the start codon. *Office Action, page 5, lines 15-17.*

The Applicants cannot understand what is gained by citing a reference that discloses a tagging vector for gene expression in mammalian cells. The Examiner must recognize that the present application deals with epitope tags in primers. Hosfield *et al.* deals solely with epitope tagging vectors, not PCR primers. Furthermore, the Examiner's emphasis on the demonstration in Figure 1 of Hosfield *et al.* "that the markers are 3' of the start codon" is misplaced – it is simply a cloning vector. Again, the Examiner is resorting to art that is not in the relevant field of endeavor and does not address the problems solved by the present invention. That is to say, Hosfield *et al.* is non-analogous art and improper art for an obviousness rejection.

c) The present rejection is clearly the result of impermissible hindsight driven analysis.

The Examiner's attempts to argue that one skilled in the art would find missing elements of the claims in references that are in a different field of endeavor and address different problems suggests that the Examiner is using hindsight:

> "To imbue one of ordinary skill in the art with knowledge of the invention . . ., when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher."

W. L. Gore & Assoc. v. Garlock, Inc., 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983). The only similarity that these references seem to have in common – excluding Hosfield *et al.* – is the use of PCR primers. But this is not enough. PCR is used in many different contexts, since it is the basic assay for making more nucleic acid out of small amounts. What one then does with the amplified nucleic acid is the question. The Examiner's combinations completely ignore this question.

II. Claims 1, 9, 11-13 and 38-41 are not unpatentable under 35 U.S.C. §103(a).

The Claims are rejected as obvious over Little *et al.* in view of Garvin *et al.* and further inv view of Nakajima *et al.* and Hosfield *et al.* and further in view of Elion *et al.* Based on the above arguments regarding Nakajima *et al.* and Hosfield *et al.* the Applicants likewise contend

that the rejection of Claims 1, 9 and 11-13 based on a further combination with Elion should be withdrawn. Elion is only cited by the Examiner as allegedly teaching primers of certain lengths. Elion does not remedy the above-indicated deficiencies of the combination of Nakajima *et al.* and Hosfield *et al.* with Little/Garvin.

CONCLUSION

In view of the above arguments and amendments, the Applicants contend that Claims 1, 9 and 11-13 as well as new Claims 38-41 are in condition for allowance. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned at 781.828.9870

Respectfully submitted,

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